



Princess Nora Bint Abdul Rahman University

College of Medicine

My child is bed wetting

Case-2; Tutor guide

Year 2 (level 4)

Endocrinology block

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Case-2; Tutorial-1

Trigger

40 minutes

Karima Ahmed, a 3-year-old girl, started wetting her bed at night for the last two weeks. Her mother, Suha, was very upset because Karima had been potty trained one year ago. Her sister, Haifaa a second year medical student, suggested to consult a pediatrician as her mother was highly concerned about this unexplained regression. The mother preferred to ask the family doctor "Dr. Faisal" about the possible cause of Karima's condition.

During their visit to Dr. Faisal's clinic, Suha reported that Karima was clingy, whiny and did not want to play in the last few weeks. She was always thirsty and need to drink fluid most of the time. Besides bed-wetting at night, Karima was using the bathroom often during the day.

When asked, the mother denied the presence of any recent events that would have a direct psychological effect on Karima.

Discussion Questions:

- Are there any difficult words you do not understand?
- List the key information about Karima.
- Identify Karima's presenting problems
- For each problem make a list of how it may be caused (generate hypotheses)
- What further information would you like to know to help you differentiate between your hypotheses?

New terms:

Clingy: adherent; wanting to be with her mother all the time in a way that is annoying

Whiny: noisy; complaining

Hypotheses:

Bedwetting at night (Secondary nocturnal enuresis):

- Nocturnal polyuria: as in Anti-diuretic hormone (ADH) deficiency [Diabetes insipidus], diabetes mellitus, caffeine rich fluid, e.g. excess Coca drinking, and medications.
- Bladder infection, mainly cystitis.
- Psychological stress, such as birth of a new sibling, parental divorce or separation, death in the family, or problems at school.
- Constipation also can be a cause or an aggravating factor. Full bowels press on the bladder, and can cause uncontrolled bladder contractions, during waking or sleep
- Obstructive sleep apnea due to large adenoids may leads to nocturnal enuresis.
- **Overactive bladder**, children often have to run to the bathroom by day too [Usually not secondary]
- Deep sleeper: a problem with waking-up to the sensation of a full or contracting bladder [Usually not secondary].

She was clingy, whiny and did not want to play:

- Severe/recurrent infection
- Increased metabolic needs, e.g. Diabetes Mellitus, impaired thyroid function or growth hormone deficiency
- Cardiac disorders, such as congenital heart defects
- Pulmonary disorders, such as chronic lung disease
- Malignancy
- Renal disease, such as renal failure [Rare in this age]
- Psychological

She is always thirsty

- Physiological: Eating salty or spicy meals/ Extremely hot weather
- Diabetes Mellitus
- Diabetes insipidus
- Medications such as diuretics
- Loss of body fluids: as in severe infections (sepsis) or burns, or heart, liver, or kidney failure
- A mental disorder called psychogenic polydipsia

Facilitation Questions:

What are the information needed to help differentiate between the different hypotheses?

I. From medical history questions may include:

- Is she eating more salty or spicy foods recently?
- Has the mother noticed an increase in Karima's appetite?
- Has the mother noticed an unintentional weight loss?
- Is Karima producing more or less urine with each voiding? And if this is accompanied by burning sensation or not?
- Did the mother notice any bleeding in urine or darker than normal in color?
- Is Karima sweating more than usual?
- Does she developed fever in the last two weeks?

II. Tests that may be ordered include the following:

- | | | |
|-----------------------|---------------------------------------|--------------------|
| - Blood glucose level | - CBC and blood differential | - Serum osmolality |
| - Serum sodium | - Urine analysis and urine osmolality | |

History & Examination

40 minutes

Past history

Dr. Faisal reviewed Karima's medical record. She is a full term baby and her perinatal history was irrelevant. She did not experience any serious medical illness since birth and has no known allergies. Karima's growth was normal as well as her developmental skills in accordance to her age. She received all immunization as scheduled.

Family history:

Karima has two sisters and a brother. As recorded in the file, Mr. Ahmed, Karima's father is a known diabetic and is taking oral hypoglycemic drugs for the last 15 years. Suha had gestational diabetes and delivered a stillborn baby last year. Karima's paternal grandfather is diabetic and hypertensive; his foot was amputated six months ago after improper healing of a foot ulcer. Haifaa added that one of her cousins who is 18 months old was recently diagnosed with Diabetes Mellitus (DM) Type 1.

Physical examination: Karima is a lean child with a mildly loose skin. She has dry mucous membranes but she is not anemic and had no palpable lymph nodes. In reference to the growth chart, her height was normal (75 percentile) while her weight showed no increase since her last well child check-up at two years of age.

Vital signs: Pulse: 85/min; blood pressure: 100/70 mmHg; temperature: 36.9°C; respiratory rate: 22/min

Systemic examination:

CVS: She had a regular heart rate and rhythm, negative for murmurs, or gallops, with normal first, second and third heart sounds.

Respiratory system: Normal vesicular breathing, no additional sounds.

Abdomen: Normal on examination with no palpable organs and the gut sounds were audible.

CNS: Sensory, motor systems and cranial nerves were intact.

Discussion Questions

- Are there any difficult words you do not understand?
- List the key information in this progress
- What is your refined hypothesis? Justify your views
- What further information would help you differentiate between your hypotheses?

Facilitation Questions:

According to the information provided, what is the most probable diagnosis?

Diabetes mellitus due to: C/P: polyuria, polydipsia [Increase thirst sensation] and loss of weight.

PE: No weight gain and dehydration. History: karima's family history increase her risk of DM.

What is the impact of the strong family history of diabetes mellitus?

Type I Diabetes has a genetic etiology, individuals has an increased risk for disease development when a relative, specifically parent or grandparent has already been diagnosed with diabetes.

Progress

40 minutes

Dr. Faisal took a urine sample from Karima and performed a rapid check using a routine dipstick that showed glucose (+++) and ketone (++) [Normal: Negative]. He explained to them that Karima might have DM type 1. Suha was highly anxious after hearing that, and Haifaa wondered about the efficacy of urine analysis as a diagnostic tool for DM. However, Dr. Faisal reassured them and asked for the following investigations to confirm his diagnosis:

- Complete urine analysis
- Fasting and two hours postprandial blood glucose
- HbA1c level and
- Fasting serum C-peptide

Dr. Faisal took this opportunity to check Mr. Ahmad's random blood glucose using an automated blood glucose monitoring devices. His blood glucose was 16.6 mmol/L [Normal: 4.4 - 6.1 mmol/L]. Mr. Ahmad is taking metformin tablets as oral hypoglycemic regularly, which was titrated up to 1000 mg twice-daily. Suha added that he is not following the dietary regimen prescribed to him such as having multiple servings of dessert when going out with his friends.

Dr. Faisal advised Mr. Ahmad to perform fasting and two hours postprandial blood glucose, HbA1c, lipid profile, kidney function tests for creatinine and microalbuminuria. He also emphasized that the test results of Karima should be performed as soon as possible. Haifaa was worried about her family members and decided to read more about DM causes, predisposing factors, management and complications.

Discussion Questions

- Are there any difficult terms you do not understand?
- Summarize the key information you have obtained from this progress
- On the basis of the new information, how would you explain the condition of Mr. Ahmad and Karima
- How would the laboratory tests ordered may help confirm the cause of Karima's condition
- Should Haifaa be concerned about her family members' condition

Facilitation Questions:

What is the diagnostic criteria of diabetes mellitus?

The current WHO diagnostic criteria for diagnosis of diabetes is – fasting plasma glucose more than 7.0mmol/l (126mg/dl) and 2-hrs plasma glucose $\geq$ 11.1mmol/l (200mg/dl).

How could diabetes mellitus be responsible of Karima's symptoms, signs (polyuria, polydipsia, weight loss and dehydration) and urine results? What is the possible pathophysiology of the disease.

In type 1 Diabetes mellitus, there is deficiency of insulin secreted → there is no glucose uptake by the cells and plasma glucose levels are increased.

Excess glucose is excreted in urine → increase of urinary osmotic pressure → increase release of water in urine → increase urine volume → frequent urination “polyuria”.

As a result of excessive output, the body becomes dehydrated and the loss of fluids causes increased levels of thirst eventually leading to “polydipsia”.

The body breakdown its depot fat to be used as a source of energy. Increased free fatty acids can be oxidized by liver forming acetyl CoA that is when produced in excess result in the formation of ketone bodies that are secreted in urine in excess (Ketone urine ++).

What are the hormones that regulate normal blood glucose?

Glucose homeostasis is controlled primarily by insulin that lowers blood glucose levels. In response to glucose, insulin is secreted in a characteristic biphasic pattern: an acute first phase lasting a few minutes, followed by a sustained second phase.

Glucagon and several other anti-insulin hormones (catecholamines, cortisol, and growth hormone) oppose insulin's action. These hormones raise blood sugar levels.

What is the significance of the test ordered for Karima and Mr. Ahmad?

Regarding laboratory tests ordered for Karima:

- **Urine analysis:** to exclude urinary tract infection
 - **Fasting and two hours postprandial:** to confirm the diagnosis of DM as +ve results in urine are not diagnostic
 - **HbA1c level:**
 - ✓ It represents non-enzymatic glycosylation of normal hemoglobin [HbA]. It increases if blood glucose levels are increased, so it can give a figure on the blood glucose status in the last 3 months [the life span of the RBC's].
 - ✓ Normal level [4-5.6%]. Levels between 5.7% and 6.4% indicate increased risk of diabetes, and levels of 6.5% or higher indicate diabetes.
 - ✓ For follow up, HbA1c provides a record for whether the patient's diabetes is under control or not and to what degree diet or medication or both need to be modified.
 - **Fasting serum C-peptide:**
- C-peptide, is produced during insulin synthesis from the prohormone that splits into two pieces: insulin and C-peptide. It is measured to give an idea on the endogenously formed insulin. Low values (or no C-peptide) indicate that the pancreas is producing little or no insulin.

Regarding laboratory tests ordered for Mr. Ahmed:

- Fasting, two hours postprandial blood glucose, and HbA1c: for follow up for compliance to treatment and effectiveness of the oral hypoglycemic drugs.

- Lipid profile, kidney function tests for creatinine and microalbuminuria: to check for presence of any chronic complications of diabetes mellitus

Chronic complications of DM include:

Hyperglycaemia has an important role in the pathogenesis of diabetic complications by increasing protein glycation and the gradual build-up of advanced glycation endproducts (AGEs) in body tissues. These AGE form on intra- and extracellular proteins, lipids, nucleic acids and cross-linking with these molecules. Protein glycation and AGE are accompanied by increased free radical activity that contributes towards the biomolecular damage in diabetes. Interaction of AGEs with their receptors alter intracellular signalling, and cause release of pro-inflammatory molecules and free radicals that contribute towards the pathology of diabetic complications. AGEs is now considered to have a major role in the pathogenesis of DM complications.

Chronic elevation of blood glucose level leads to damage of blood vessels (angiopathy). In diabetes, this results into "microvascular disease" (due to damage to small blood vessels) and "macrovascular disease" (due to damage to the arteries). Example of chronic complications of DM:

- ✓ Increase risk of atherosclerosis with high risk of Coronary heart disease.
- ✓ Cerebrovascular disease, which can lead to stroke
- ✓ Retinopathy, which can lead to blindness
- ✓ Nephropathy, which can lead to kidney failure and the need for dialysis
- ✓ Peripheral neuropathy, mostly resulting in loss of sensation of the foot. Any wound may progress to ulceration → diabetic foot that might require amputation

What is the pathogenesis of Diabetes mellitus?

Type 1 DM, may be caused by the following:

1. **Immune-mediated:** This form of diabetes, which accounts for only 5–10% of those with diabetes, previously encompassed by the terms insulin-dependent diabetes, type I diabetes, or juvenile-onset diabetes, results from a cellular-mediated autoimmune destruction of the B-cells of the pancreas. One and usually more of these autoantibodies are present in 85–90% of individuals. In this form of diabetes, the rate of B-cell destruction is quite variable, being rapid in some individuals (mainly infants and children) and slow in others (mainly young adults). Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. Others have modest fasting hyperglycemia that can rapidly change to severe hyperglycemia and/or ketoacidosis in the presence of infection or other stress. Autoimmune destruction of B-cells has multiple genetic predispositions and is also related to environmental factors that are still poorly defined.
2. **Idiopathic diabetes:** Some forms of type 1 diabetes have no known etiologies. Some of these patients are prone to ketoacidosis, but have no evidence of autoimmunity. Although only a minority of patients with type 1 diabetes fall into this category, of those who do, most are of

African or Asian ancestry. Individuals with this form of diabetes suffer from episodic ketoacidosis and exhibit varying degrees of insulin deficiency between episodes. This form of diabetes is strongly inherited, lacks immunological evidence for B-cell autoimmunity.

In type 2 DM, there are two main pathophysiological defects: 1) impaired insulin secretion through a dysfunction of the pancreatic β -cell, and 2) impaired insulin action through insulin resistance.

Although the mechanisms underlying the β -cell dysfunction remain unclear, they are likely to be multifactorial. As well as genetic factors, a number of environmental factors (including early-life malnutrition and obesity) and hyperglycaemia and hyperlipidaemia per se may all accelerate the decline in β -cell function.

In addition, the β -cell responds to insulin resistance by increasing insulin secretion to compensate and to maintain glucose concentrations within the normal range. The maximal insulin secretory capacity is eventually reached and, beyond that point, insulin secretion declines. By this time, oral hypoglycemic drugs are not sufficient and exogenous insulin may be introduced as treatment.

What is the effect of metformin as oral hypoglycemic drugs?

There are two classes of oral hypoglycemic drugs that directly improve insulin action: biguanides (including metformin is currently available) and thiazolidinediones. Metformin is considered the first choice for oral treatment of type 2 diabetes.

Mechanism of action:

Metformin is effective only in the presence of insulin, and its major effect is to decrease hepatic glucose output. In addition, metformin increases insulin-mediated glucose utilization in peripheral tissues (such as muscle and liver), particularly after meals, and has an antilipolytic effect that lowers serum free fatty acid concentrations.

Case-2; Tutorial-2

Discussion of learning issues

60 minutes

The students will discuss the learning issues identified in tutorial one in about 60 minutes. A scribe on the whiteboard is needed to help in this process.

Once completed, the group may progress to the next section.

Progress 1:

20 minutes

Very next day after their visit to the family doctor, Karima developed fever and cough with inability to eat or drink. Haifaa suggested to give her antipyretics till they get the investigations results and then consult Dr. Faisal. At night, Haifaa noticed that her sister is drowsy and confused; she also smelt a fruity odor from her mouth. Mr. Ahmad took Karima to the ER in King Khaled hospital in semi-conscious state. On examination, her breathing was deep and rapid with acetone smell and respiratory rate was 24/min. Pulse rate was 100/min, blood pressure 100/70 mmHg and temperature 38.5° C. She also had signs of dehydration. Rapid hematology and biochemical tests showed the followings:

Hemoglobin: 12.9 g/dl	Hematocrit: 44%	TLC: 12,000/μl
Random blood glucose: 28.9 mmol/L (N: 4.4 - 6.1 mmol/L)		
Serum ketones: 2+ on undiluted serum		
Serum urea: 50 mg/dl (N: 20-40)	Serum Creatinine: 0.8 mg/dl (N: 0.4-1.2)	
Serum electrolytes and blood gases:		
Sodium: 152 mEq/L (N: 135-145)	Potassium :4.7 mEq/L (N: 3.5-5)	
Chloride: 95 mmol/L (N: 95-105 mmol/L)	Bicarbonate: 12 mEq/L (N: 21-28)	
Arterial pH: 7.1 (N: 7.35-7.45)	PaO ₂ :95 mmHg (N: 80-100)	
PaCO ₂ : 28 mmHg (N: 35-45)	O ₂ saturation: 98% (N: 95-100)	
Calculated anion gap was 45 mEq/L (N: 3-11)		

The diagnosis of diabetic ketoacidosis was made.

Discussion Questions

- Summarize the key information you have obtained from this progress
- How would you explain Karima's condition and the cause of this complication?

Facilitation Questions:

How can you identify a case of Diabetic ketoacidosis (DKA)?

Ketoacidosis is an acid-base imbalance caused by an increase in concentration of ketones in the blood. This is a severe form of hyperglycemia and is life threatening in many individuals with type 1 diabetes.

Symptoms that commonly occur include nausea and/or vomiting, fruity or acetone breath, Kussmaul respirations, and mental status changes. This can occur when adequate insulin is not

available which stimulates glucose production via gluconeogenesis and lipolysis by counter-regulatory hormones in an attempt to avoid starvation.

Ketone bodies are produced in the liver from acetyl-CoA liberated during lipolysis from fatty acids. Three ketone bodies are produced: acetone (resulting in the fruity odor of DKA patients), aceto-acetate and β -hydroxybutyrate (β -OHB). β -OHB is the most prominent contributor to metabolic acidosis in patients with DKA. Acetone does not contribute to acidosis and is not usually measured as such, but it is volatile and is diagnostic for DKA by evaluating the odor of breathing and patient's urine. Blood ketones can be measured with capillary finger prick blood. This measures β -OHB directly and accurately and a value of 3 mmol/l and above has a positive likelihood ratio for the presence of DKA.

Accumulation of ketones in the bloodstream, with glucose, causing osmotic diuresis, which results in dehydration and electrolyte imbalances.

An arterial pH of less than 7.3 should be present in the diagnosis of DKA. The measurement of pH and/or serum bicarbonate is essential for the diagnosis and estimation of severity of DKA. The pH is also an important measure to assess improvement and for adjustment of treatment.

What are Diagnostic criteria of Diabetic ketoacidosis (DKA) and how to evaluate the case?

	Mild	Moderate	Severe
Plasma glucose (mmol/L)	> 13.9	> 13.9	> 13.9
Arterial pH	7.25–7.30	7.00–7.24	< 7.00
Serum bicarbonate (mmol/L)	15–18	10–14.9	< 10
Urine ketones	Positive	Positive	Positive
Serum ketones	Positive	Positive	Positive
Anion gap	> 10	> 12	> 12
Sensorium	Alert	Alert/drowsy	Stupor/coma

What are the precipitating factors that can trigger DKA?

- The most common precipitating event for the development of DKA is infection, which accounts for 28 to 45% of cases. Pneumonia or any lung disease that can influence oxygenation, and can lead to respiratory failure, should always be considered as extremely serious because it may impair respiratory compensation of metabolic acidosis. Other infection can be genito-urinary and septicaemia.
- The second most common precipitating event worldwide is the omission of insulin.
- The third most common cause is the first manifestation of new onset diabetes.
- Other common precipitating events include cardiovascular events such as a stroke, myocardial infarction and peripheral vascular disease with gangrene.

Management:

20 minutes

Rehydration have been initiated with normal saline (NaCl 0.9%) in light of initial laboratory data. Insulin therapy was begun with regular insulin infused intravenously at a rate of 0.1 unit/kg/hour with a syringe pump.

10 mEq of potassium were given to each liter of normal saline infused. Serum potassium was monitored throughout the therapeutic course to maintain its level within normal physiological range.

The blood glucose had fallen to 16.6 mmol/L three hours after admission, and reached normal levels eight hours after the initiation of therapy.

Diet and activity

A comprehensive diet plan advised with help of a professional dietitian

- A daily caloric intake prescribed
- Recommendation for amount of dietary carbohydrates, fats and proteins
- Instructions on how to divide calorie between meals and snacks
- Exercises advised

Discussion Questions

- How would you evaluate the management given to her?
- What is the plan of management for life-long treatment of Karima?

Facilitation Questions:

What is the appropriate management of DKA?

The treatment of a patient with new onset type 1 DM involves medical therapy, family education and support.

Treatment for DKA requires admission to the intensive care unit for IV rehydration, insulin drip therapy and close monitoring of vital signs, neurochecks, blood gases, blood glucoses and electrolytes.

What is the plan of management for life-long care of Karima?

The entire family should be educated on the pathophysiology and treatment of type 1 DM from the first day of diagnosis. Parents and patients should learn life skills, which include blood glucose testing (using their home glucose monitor), giving injections of insulin and monitoring urinary ketones. The family learns how to recognize and treat emergencies like hypoglycemia and hyperglycemia. The dietitian should teach the newly diagnosed family about how foods influence blood sugars and how the other nutrients are involved in balancing the meal. In addition, the family members should know that the social stability of the family is highly important.

An endocrinologist has to make sure that the patient will be smoothly transferred from hospital to home. A hospital stay is typically at least two days and nights, which allows for stability of blood sugars before going home.

Progress 2:

20 minutes

She was advised to continue insulin injection subcutaneously before breakfast and supper. Suha was taught by the doctor how to inject Insulin subcutaneously and what are the proper sites for injections. Karima will have regular follow up with Dr. Hanadi, a pediatrician, for additional education, meal plan and life-long treatment.

Mr Ahmad got his laboratory investigations results that were highly elevated as shown below:

Fasting Blood Glucose: 13.8 mmol/L (N: 3.8 - 6.1 mmol/L)
Two hours postprandial blood glucose: 22.2 mmol/L (N: 3.8- 6.9 mmol/L)
HbA1C: 11.2% (N: 4-5.8 %)
Kidney functions:
Serum Creatinine: 1.5 mg/dl (N: 0.4-1.4 in male)
Serum urea: 55 mg/dl (N: 20-40)
Microalbuminuria: 275 µg/mg creatinine (N: Less than 30)
Lipid profile:
Serum Total Cholesterol: 300 mg/dl (N below 50 yrs: 150-200; above 50 yrs: 150-240)
Serum Triglycerides: 250 mg/dl (N: 90-150)
HDL: 30 mg/dl (N in men: 45-65)
LDL: 220 mg/dl (N: 60-130)

During these days, Haifaa read extensively about DM, as she was much anxious about her family especially about her father. She was suspicious that her father is at risk of developing serious complications of DM due to non-compliance to the medications and inappropriate dietary habits, especially with their positive family history of DM. She decided to consult an endocrinologist for appropriate management of her father and his follow up.

Discussion Questions

- What are the different complications that Haifaa is worried about?
- Based on your knowledge, what are your suggestions to avoid chronic complications of DM?
- What are the health education interventions and monitoring parameters needed to achieve the best prognosis for the disease?

Facilitation Questions:

What is the significance of microalbuminuria?

Microalbuminuria is defined as excretion of 30–300 µg of albumin per mg creatinine. The detection of microalbuminuria has been linked to the identification of incipient diabetic kidney disease. This phase calls for aggressive management to prevent or retard overt diabetic nephropathy. Annual screening for microalbuminuria is indicated for all individuals with diabetes mellitus.

Reference values of Microalbuminuria:

Less than 30 µg/mg creatinine: Normal

30-300 µg/mg creatinine: Microalbuminuria

More than 300 µg/mg creatinine: Macroalbuminuria

According to the laboratory results, What are the complications that Mr. Ahmed is at high risk of?

1. Diabetic atherosclerosis

Atherosclerosis is the most serious consequence of long-term diabetes and the major cause of death in these patients. It is characterized by deposition of atherosclerotic plaques on the insides of arterial walls, occlusion of blood flow and eventual myocardial infarction.

- Increased glycation of low-density lipoprotein (LDL) occurs in diabetes. Glycated LDL is not recognized by the LDL receptor but its uptake by macrophages is enhanced and this may account, at least in part, for the hyperlipidaemia and accelerated foam cell formation observed in diabetic patients.
- LDL is also modified by advanced glycation endproducts (AGE) and this LDL-AGE increases in diabetic patients and has reduced serum clearance.
- Glycation and AGE formation are also accompanied by increased oxidation of LDL and an increase in this atherogenic oxidized LDL occurs in diabetes. On the other hand, glycation of high-density lipoprotein (HDL) increases its turnover and reduces its efficiency during reverse cholesterol transport.
- Furthermore, AGEs promote secretion of several cytokines that not only control migration of monocytes and macrophages but also promote proliferation of smooth muscle cells, an important step in atherosclerotic plaque formation.

2. Diabetic nephropathy:

Diabetic nephropathy is characterized by a thickening of the basement membrane, expansion of the mesangium, reduced filtration, albuminuria and ultimately renal failure.

- AGEs have been detected in renal tissues in amounts that has been correlated with the severity of diabetic nephropathy. Hyperglycaemia and AGEs increase the release of transforming growth factor- β (TGF- β) which in turn stimulates synthesis of collagen matrix components and this may account for, at least in part, the thickening of the basement membrane in diabetic nephropathy.
- The accumulation of AGEs on collagen in the basement membrane together with their ability to trap plasma proteins may also contribute towards thickening of the basement membrane, altered filtration and ultimately loss of glomerular function.
- The reduced filtration in diabetic nephropathy is, in part, due to an expansion of the mesangial layer that causes compression of capillaries and a reduction in the surface area over which filtration takes place.

- AGEs can form on serum proteins and small peptides in the circulation. These circulating AGE-peptides are normally cleared by the kidneys but this does not occur in diabetic nephropathy where their serum concentration rises.
- Patients with chronic renal failure have a higher incidence of cancer. This may be due to increased intracellular free radical activity capable of damaging DNA following interaction of AGEs with its receptor.

What are the healthy regulations that a diabetic patient should follow beside treatment?

- Reducing breakfast carbohydrates and exercising after breakfast both may help to reduce the post-breakfast glucose elevation that this patient may experience. The patient should eat less cereal and to reduce the quantities of milk and juice.
- Depending on the patient schedule, he/she can exercise before or after breakfast. Exercise increases insulin sensitivity, and the effect lasts for several hours.
- Patients should avoid skipping a meal altogether, which has been found to be associated with weight gain. Skipping dinner would lower mostly bedtime and overnight glucose levels.

LEARNING ISSUES:

1. Identify the cellular structure and functions of endocrine pancreas
2. State the normal glucose homeostasis and recognize the type, functions and regulation of glycemic hormones.
3. Discuss the etiology, pathogenesis and clinical presentation of the different types of diabetes mellitus
4. Discuss the predisposing factors and possible acute and chronic complications of diabetes.
5. Prepare a management plan of a patient with Diabetes mellitus type 1 and type 2 and recognize the mode of action and indications of hypoglycemic drugs in each type.
6. Advise a dietary plan for a diabetic patient with emphasis on foods that should be avoided